Correlation Duration of Oral Steroids Drug Administration by Intraocular Pressure in Patients with Systemic Lupus Erythematosus (SLE) in Dr. Mohammad Hoesin General Hospital Palembang

Syarif Satya Graha[1], Fidalia[1], Prima Mayasari[1], Nova Kurniati[2], Irsan Saleh[3]*

[1]Ophthalmology Departement, Moh.Hoesin General Hospital, Palembang, Indonesia
[2]Internal Medicine Department, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[3]Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ABSTRACT

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease and multisystem organ involvement. SLE patients given treatment are manifold, one of which is with steroids. Long time drug administration depends on the clinical condition of the patient. Oral steroids may cause an increase in intraocular pressure, depending on the type of steroid that is administered, the route of administration and duration of taking the medication. To determine the correlation length of oral steroid drug administration by intraocular pressure in patients with SLE in dr. Mohammad Hoesin general hospital (RSMH) Palembang. This study was an observational study exploratory. Intra-ocular pressure examination uses Goldmann Tonometry Aplanation in patients with SLE who use oral steroid medication (methylprednisolone) in RSMH Palembang. Data were analyzed with correlation. Hypothesis test results correlation between duration of oral steroid drug (metylprednisolone) with intraocular pressure in patients with SLE using Spearman Correlations test obtained r = 0.054 and p = 0.637. There was no significant correlation between the duration of oral steroid medication (methylprednisolone) with intra-ocular pressure in patients with SLE. But looks very weak correlation strength.

Key words: Intraocular pressure, metylprednisolone, Steroid induced glaucoma, Systemic Lupus Erythematosus (SLE).

INTRODUCTION

Intraocular pressure (IOP) is a biological entity that shows daily fluctuations. IOP is required for normal vision which ensures the clearness of eye media and the constant distance between cornea with lens and lens with retina [1-5] Corticosteroids can cause glaucoma by elevating IOP with open angle mechanisms. The mechanism is associated with a double effect on trabecular meshwork, another mechanism leading to cytoskeletal changes that may inhibit pinocytosis from the aqueous humor. Corticosteroids also lead to a decrease in prostaglandin synthesis that regulates excretion of aqueous humor that resulting in increased IOP causing pressure on the optic nerve and causing visual disturbance and visual nerve damage [6-10].

Increasing of IOP incidence caused by systemic steroid consumption is not known for sure because most of these sufferers do not do IOP examination. These sufferers may be found during routine eye examinations [6, 7]. One of the systemic diseases that commonly use corticosteroid therapy in its treatment is Systemic Lupus Erythematosus (SLE) disease which is a chronic autoimmune disease and has multisystem organ involvement. Eyes are not the primary target of SLE mediated by immune disorders, but can affect significant ocular morbidity. Ocular disorders due to side effects of steroid use are often overlooked by health personnel so that

diagnosis and treatment are delayed causing visual loss and permanent damage [11-15]. From the description and the absence of previous studies that detect the correlation of the duration of oral steroid administration with increased IOP in patients with Systemic Lupus Erythematosus (SLE) causes researcher to study whether there is a correlation between the duration of corticosteroid therapy with incidence of increased IOP in patients with SLE. With the results of this study is expected to know the increase in IOP due to long-term steroid administration so that can be prevented eye damage due to corticosteroid therapy in patients with SLE.

MATERIAL AND METHODS

This study was an observational analytic with cross sectional design to know the correlation of duration of oral steroid drug administration with increasing of IOP in SLE patient. This study was conducted at dr. Mohammad Hoesin general hospital in Palembang. Duration of study was from September 2015 to December 2015. The population was all patients diagnosed with SLE at Dr. Mohammad Hoesin general hospital Palembang. Sample was all patients diagnosed with SLE receiving steroid therapy at dr. Mohammad Hoesin hospital that meets inclusion and exclusion criteria. The number of samples in this study amounted to 78 samples. The inclusion criteria in this study was all patients diagnosed with SLE and willing to follow the study stated by signing an informed consent, all patients diagnosed with SLE who received oral steroid therapy (methylprednisolone) > 6 weeks on a regular basis and patients diagnosed with SLE who had no history of the use of antiglaucoma medications or drugs that can decrease IOP. The exclusion criteria in this study was patients diagnosed with SLE with a history of eye trauma and eye surgery, patients diagnosed with SLE who had systemic diseases such as diabetes mellitus, patients diagnosed with SLE who had anterior and posterior segments such as uveitis, cataract , optic neuropathy and patients diagnosed with SLE on gonioscopic examination have closed or narrow angle. The independent variable in this study was the duration of oral steroid used while the dependent variable in this study was intraocular pressure, posterior segment state and field disturbance. After data collected, the data was analyzed univariat and bivariate. Bivariate analysis used Spearman's correlation test. Data analysis was calculated by using computer program that was SPSS (Statistical Program for Social Science).

RESULTS

Primary data was obtained from patients in the internal medicine polyclinics who diagnosed SLE and consulted to ophthalmology polyclinic subdivision glaucoma in Dr. Mohammad Hoesin hospital. The sample was taken by consecutive sampling. The type of steroid administered to all SLE patients was methylprednisolone at a dose varying from 4 mg daily to 48 mg daily with the duration of administration which also varied from 9 weeks to 952 weeks.

General Characteristics of Research Subjects
General characteristics of this study encompassed gender, age, education and occupation. Based on table 1, the number of respondents was dominated by women as many as 75 people (96.2%). The largest age group was 30-39 years old as many as 34 people (43.6%) and the lowest age group was <19 years as many as 6 people (7.7%). Most of the samples of this study were women as much as 96.2%. This corresponds to Bertsias et al, which said women tend to suffer from SLE as much as nine times greater than men. Based on study conducted by Somer et al, that the incidence of SLE in women is higher than males is 6.2: 1. According to Uramoto et al, this is due to the high estrogen factor in women can trigger the occurrence of SLE [16-18] Most of the subjects of this research were 30-39 years old. The results of this study were consistent with Menachem, that the peak onset of SLE occured at age 15 to 40 years. Study conducted by Somer et al, stated that SLE occured between the ages of 22 to 55 years with an average age of 39 years. Study conducted by Costenbader et al, showed that women who are reproductive age, especially during menarche and approaching menopause have a greater risk for SLE [17,19,20].

Vision characteristics
Based on table 2, the baseline vision of this study was performed using LogMAR with the most baseline vision was 0.0 - 0.5 as many as 47 people (60.2%), and 31 samples (39.2%) with refractive anomalies. After refractive anomaly was corrected (BCVA), then the subject's vision was 0.0 with LogMAR being 78 people (100%). One of the predisposing factors of increased intra ocular pressure in patients receiving steroid therapy is high myopia. This is evidenced by study conducted

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by Gatson *et al*, showing that patients with autoimmune and connective tissue disease tend to experience "steroid responders". In this study all samples who had refractive anomaly and after have done BCVA, there was no one experienced high myopia [21-24].

Table 1: General characteristics of study subjects

Characteristics	N	%
Gender		
Male	3	3,8
Female	75	96,2
Age		
<19 years	6	7,7
20-29 years	31	39,7
30-39 years	34	43,1
≥ 40 years	7	9,0
Education		
Elementry	0	0
Junior high school	0	0
Senior high school	36	46,2
University	42	53,8
Occupation		
Civil servent	10	12,8
Enterpreneur	2	2,6
Housewife	37	47,4
Employees	18	23,1
Student	11	14,1

Table 2: Vision characteristics

Characteristics	N	%
Baseline vision (LogMAR)		
0,0 – 0,5	47	60,2
0,5 – 1,0	31	39,8
Vission after correction (BCVA) (LogMar)		
0,0	78	100

Table 3: Characteristics of intra ocular pressure

Characteristics	N	%
Normal (10-21,9)	77	98,7
Low (10-16)	30	38,5
Moderate (16,1-18)	34	43,6
High (18,1-21,9)	13	16,7
High (≥22 mmHg)	1	1,3

Characteristics of Intraocular Pressure

The intraocular pressure in this study was divided into normal and high IOP. IOP is said to be normal if the pressure is between 10 mmHg to 22 mmHg and is said to be high if the pressure is ≥22 mmHg. Normal IOP is subdivided into low, moderate and high. Based on table 3 in this study, respondents who have high intraocular pressure was only 1 sample and the rest normal. The use of steroids does not always result in glaucoma but may only lead to an increase in IOP. Increased IOP above normal that occurred in one sample, there was no

abnormalities in optical disks, retinal nerve fiber layer or field deformity [6,14].

Anterior Chamber Angle Characteristics

Anterior chamber angle that opened in this study was divided into grades III and IV. Based on table 4, samples who had grade IV were 74 samples and the rest grade III.

Table 4: Anterior chamber angle characteristics

Characteristics	N	%
Opened	78	100
Grade III	4	5,1
Grade IV	74	94,9

Most of the subjects of this study had grade IV where the tendency for increased IOP due to steroid consumption was through an open angle mechanism. Individual with pre-existing primary angle glaucoma has a much greater potential for increased IOP that induced by corticosteroid consumption. Conversely, normal individual who is classified as high steroid responders is more likely to develop into primary open-angle glaucoma. Patients with chronic primary angle closure and patients with secondary open-angle glaucoma have the same chances as in normal people who are associated with steroid responders [14,15].

Visual Field Defect Characteristics

In this study only one sample who had a high IOP and after done Humphrey Field Analyzer the result was not obtained visual field defect.

Characteristics of Dosage and Duration of Steroid Administration

In this study, steroids administered to SLE patients was methylprednisolone, consisting of 1 x 4 mg, 1 x 8 mg, 1 x 16 mg, 2 x 4 mg, 2 x 8 mg, 2 x 16 mg and 3 x 16 mg. Based on Table 5, the most widely used dose of steroid is 1 x 4 mg (38.5%). then researcher equalized a dose of methylprednisolone with prednisone. 1 x 4 mg methylprednisolone is equivalent to prednisone 6 mg, 1 x 8 mg and 2 x 4 mg methylprednisolone are equivalent to dose of prednisone 12 mg, 1 x 16 mg and 2 x 8 mg methylprednisolone are equivalent to a dose of 24 mg prednisone, 2 x 16 mg methylprednisolone is equivalent to 48 mg dose of prednisone, and 3 x 16 mg methylprednisolone is equivalent to prednisone dose of 72 mg. After that the equivalent of the dose is categorized into a low dose, moderate dose and high doses. Based on table 6, most samples

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who consumed steroids included in the moderate category (12 mg - 24 mg) as many as 43 people (55.1%). Based on table 7, samples who consumed low and moderate doses of steroids did not have high IOP. samples who consumed high dose of steroid had 1 sample who had high IOP. In this study, the duration of steroid administration was calculated from first oral steroid therapy until examination at opthalmology Polyclinic Subdivision Glaucoma Dr. Mohammad Hoesin General Hospital Palembang. Based on table 8, the duration of steroids was calculated in weeks with an average value of 134.12 weeks and a standard deviation of 167.416 weeks.

Bernstein and Schwartz examined the long term use of systemic steroids and found that there was an increase in IOP in the group with systemic steroid treated patients compared with age and sex in the control group, then it was reported that those who received steroid systemic therapy over 4 years was significantly improve IOP compared to systemic steroid usage of less than one year [27].

Table 5: Dose of steroid characteristics (Methylprednisolone)

Characteristics	N	%
1x 4 mg	30	38,5
1x8 mg	20	25,6
1x16 mg	9	11,5
2x4 mg	8	10,3
2x8 mg	6	7,7
2x16 mg	2	2,6
3x16 mg	3	3,8
Total	**78**	**100**

Table 6: Prednisone dose equivalence characteristics

Characteristics	N	%
Low dose (6 mg)	30	35,5
Moderate dose (6-24 mg)	43	55,1
High dose (48-72 mg)	5	6,4

Table 7: Characteristics of the prednisone dose equivalence category for intra ocular pressure

Category of Prednisone Dose Equivalence	Intra Ocular Pressure						High	
	Normal							
	Low		Moderate		High			
	N	%	N	%	N	%	N	%
Low dose (6 mg)	7	9,0	17	21,8	6	7,7	0	0
Moderate dose (12-24 mg)	19	24,4	17	21,8	7	9,0	0	0
High dose (48-72 mg)	4	5,1	0	0	0	0	1	1,3

In this study there was one person with SLE who had elevated IOP> 22 mmHg, Patient has taken this drug for 74 weeks with varying doses since starting to take medication until the time of IOP examination. Patients with SLE who received methylprednisolone therapy also received "corticostreoid sparing agent" that is the term used on the drug given to facilitate lower doses of corticosteroids and also function to control the underlying disease. Drugs that are often used as sparing agents are azathioprine, mycophenolate mofetil, cyclophosphamide and methotrexate. In SLE patients in this study the given agent sparing was mycophenolate mofetil (Cellcept®), this drug reportedly did not affect the IOP and also other ophthalmological disorders.

Table 8: Duration of steroid administration characteristics

Characteristics	Duration of Steroid Administration (Week)
Number of Samples	78
Maximum Value	952
Minimum Value	9
Mean	134,12
Standard Deviation	167,416

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Based on the results of hypothesis testing that there was no correlation between the duration of steroid administration in patients with SLE and IOP. This referred to the value of p-value on Spearman test of 0.637 so it could be concluded that there was no correlation between the duration of steroid administration in patients with SLE and IOP because the value of p-value above 0.05.

Table 9: Correlation duration of oral steroids drug administration by intraocular pressure in patients with systemic lupus erythematosus

		IOP
Duration of Oral Steroids Drug Administration	Correlation coefficient	0,054
	P-Value	0,637
	Total Sample	78

Spearman Correlation Test

The result of this study is consistent with study conducted by Godel et al, that the duration of systemic steroid delivery had no relationship with elevated IOP. But study by Becker and Armaly show an increase in IOP due to topical steroid delivery. The difference in the results of this study is due to the oral administration of steroids having first pass metabolism so that the concentration of the drug is reduced before reaching the target

organ [25-29]. According to Chen, the slowest steroid administration leads to an increase in IOP given systemically [25-29]. Long term steroid administration in this study did not affect IOP; this situation was possible because of the use of steroids with low doses. In this study only one sample who experienced increased IOP and had not experienced visual field defect because of increased IOP has not pressed the optic nerve so as not to cause symptom [27,28].

CONCLUSION

IOP in patients with SLE who received oral steroid therapy (methylprednisolone) with low doses and duration of> 6 weeks of administration is still within normal limits and almost no increase in IOP. There was no correlation between the duration of oral steroid administration (methylprednisolone) with intra-ocular pressure in Systemic Lupus Erythematosus patients in Dr. Mohammad Hoesin Palembang

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